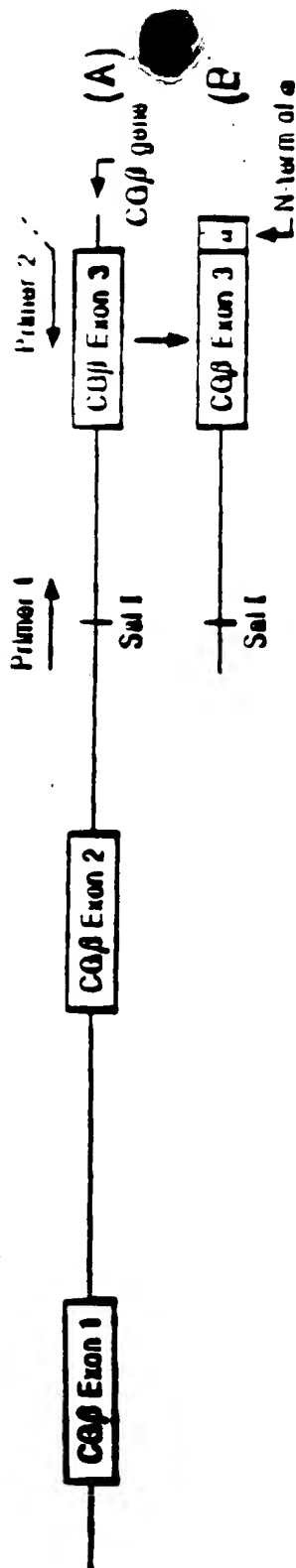
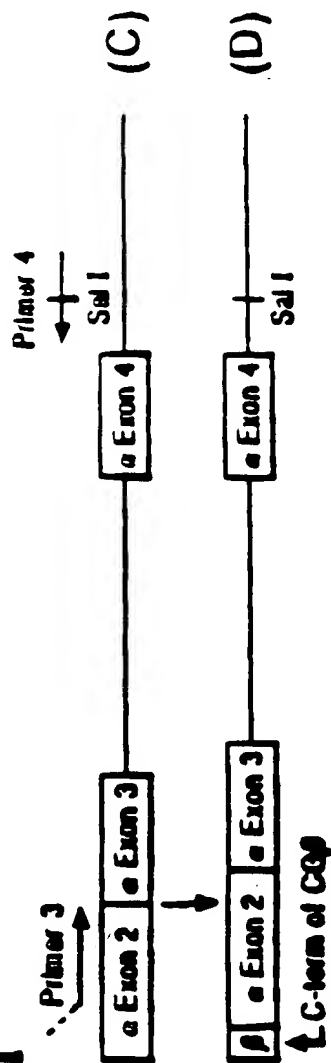


Reaction I



Reaction II



Reaction III

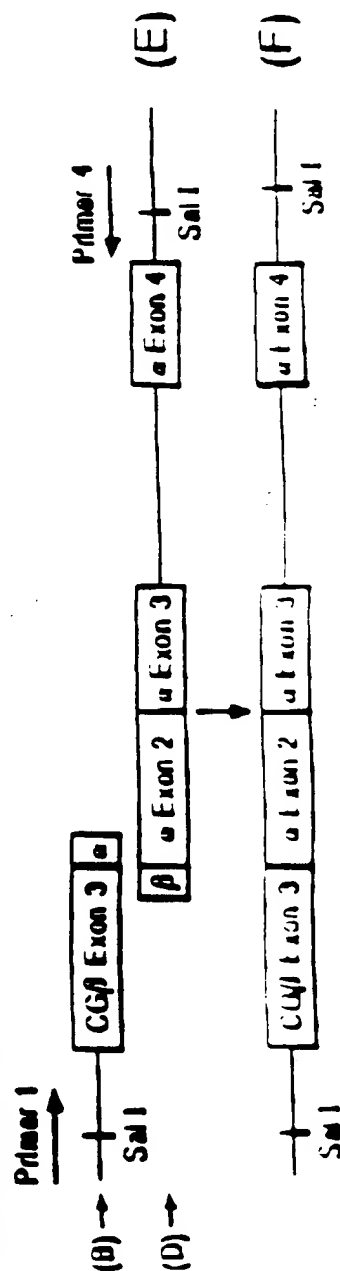


Figure 1

(hCG β -WT)

118 120 130

SerSerSerSerLysAlaProProProSerLeuProSerProSerArgLeuProGlyProSer

140 145

AspThrProIleLeuProGln

Figure 2

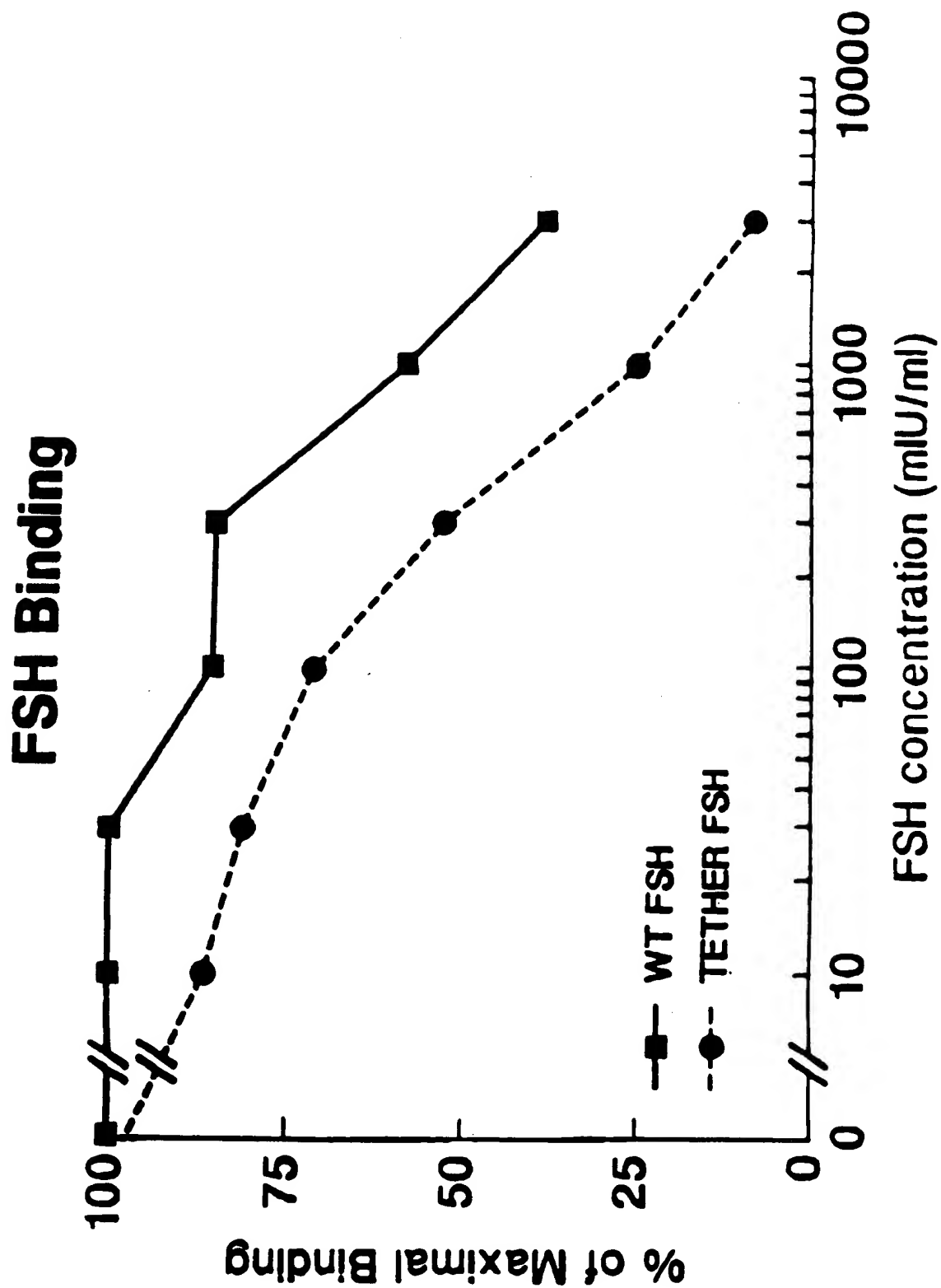


FIGURE 3

cAMP Production

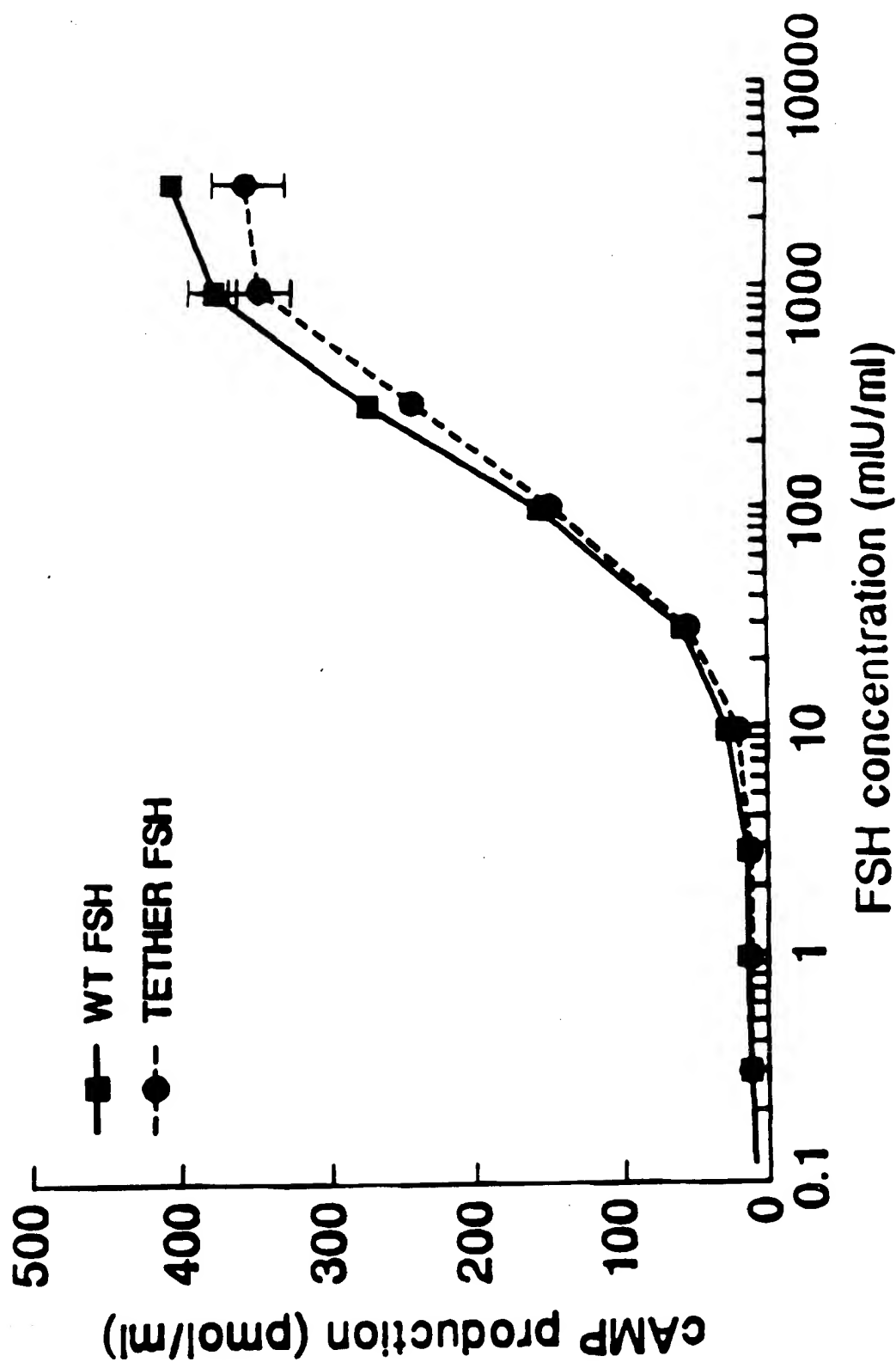


FIGURE 4

Coding Sequence for Single Chain Gonadotropin Analog #1 and Primers (underlined)

5'-ATGAATCGAGCGAATGACATCGAGCAGGATGGAGAGTGTTCAGGGGCTGCTGCTGTCTGCTGAGCATGGCGGACATGGCATCCAGGAGCGCGTTC-
 N M F Q G L L L L L L L S M G G T W A S K E P L
 3'-GGTTCCTACCTGTACAGGTCGCGAGCAGCAGCAGCAGCAGCTGTACCGGCGCTGTACCGTAGTTCCTCGGGGAA-
 ctasea(XhoI)

R P R C R P I N A T L A V E K E G C P V C I T V M T T I C A G V C P T M T
CGGGCAGGATGCGCGCCCATCATGCAACCTTGAGACAGAGAGGGGTGCCCGTGTGATCGACGTCAACACACCACTGTGCGGGTATGCTGCCCAACCATGACC-
GCCGGTCCGACCGCGGGGTAGTACGGTGGGACCGGACACACTCTCTCCGACCGGGGACACGTAGTGGCAGTGTGGTGGACACAGCGCCGATGACGGGGTGGATCTGG-

R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V M P V
CGGTGCTGAGAGGGGATCTGTGCGCCCTGCTCGAGTGTGTGCAGTATCCGCACTGCGGTTCGAGTCCATCGGGTTCCTGGGTGCCCGCGGGGTGAGCCCGTG-
GGGACAGAGTCCCCCAGAGCGCGGAGCGGAGTCCACCGAGTGTATGGCGCTACACCGCAGCTGAGTAGGCCGAGGACGACGGGGCGCGCCGACTTGGGGGAC-

cctnaga(Mat11)

V S Y A V A L S C O C A L C R R S T T D C G G P K D H P L Y C O D P R F Q
GTCTCTACGCCGTGCTCAGCTGTCATGTGCATCTGCCGCCGACGACCACTGATCTGGGGGGTCCACGACCAACCCCTGCACCTGTGATGACGCCGCCGCTTCCAG-
CAGAGGATCGCGCACCGACAGTCGACAGTACACGTGACACCGCGCGCTGTGGTGAACACCGCCGCCGAGGATCTCTGGTGGGAGACTGACACACTACTGGGGGCGAAGGTGTC-

D S S S K A P P S L P S P S R L P G P S D T P I L P Q G S G S G S
GACTCTCTCTCTCAAGGCCCTCCCCGAGCTTCCAGGCCATCCGACTCCGGGGCCTCCGACACCCGATCTCTCCCAAGGATCGGTAGCGATCTGGTAGC-
CTGAGGAGAGAGAGATTTCCGGGAGGGGGTTCCGGGAGGGTCCGAGGTTCCGGTAGGGCTGAGGGCCCCGGAGCTGTGGGGTAGGAGGGGTCTCTAGGACATCGGCTAGGACATCG-

A P D V Q D C P E C T L Q E N P F S Q P G A P I L Q C M G C C F S R A Y
GGTCTGTGATGGAGATGGCCAGATGCACGGCTACAGAAACCCATCTCTCCACGGTGGTCCCACTACTCAGTGCATGGCGTGGCTTCTCTAGACGATAT-
CGAAGATACACAGTCTTAACGGGTCTACGTGCATGCTCTTTGGGTAAAGAGGGTGGCGCCACGGGGTTAAGTCACTACCGACGACGAGGAGATCTCGTATA-
gcct(Eco47III)

P P T P L R S K K T M L V Q K N V T S E S Y C C V A K S Y M R V T V M G G F
C C C C C C T C C A T A G S T G C C A M A G A C G A T T G S T C C A A A G A C G T C A C C T C A G A G T C C A C T T G T G A G C T A A T C A T A T A C A G G T C A C A G T A T G G G G G G T T T C
G G G T A G G T G A T T C C A G G T C T T C T G C T A C A C C A G G T T T C T T C G A T G G A G T C C A G T C A G A G A C A C A T C G A T T T A G T A T A T T G T C C A G T G T C A T T A C C C C C C A A G

K V E N H T A C H C S T C Y Y H K S *

AAAGTGGAGAACACACGGGGTGGCACATGCAGTACTGTATATATCACAAATCTTAAGGTACC-3'

TTTACCTCTTGGTGTGCGGCACGGTGACGTCATGACCAATAATAGTGTTAGAAITCCATGGCCTAGGTAGAGITCGAATAGGCCCT-5'

(Kpnl)ggtagccggatcc(BglII)

Figure 6

Coding Sequence for Single Chain Gonadotropin Analog #2 and Primers (underlined):

5'-ATGAAATGAGCGGAATCAGACTGAGGACAGGATGAGATGTTCCAGGGGTGCTGCTGCTGCTGAGCATGGCGGACATGGGCATCCAGGACCGCTT-
 3'-GGTTCTTACCTCTACAAAGGTCCCGAGCGGACAGGACGAGCACTCGTACCCGCTGTACCCGTAGGTTCTCTGGCGAA-
 ctgagg(XhoI)
 M E M F Q G L L L L L L S M G G T W A S K E P L
 R P C R P I M A T L A V E K E G C P V C I T V M T I C A G Y C P T M T
 CGCCACGGTGCAGCCCATCATGCCACCTGAGTGTGAGAGAGAGGGTGCCTGGTGTGCATCAGCGTCAACACACCATCTGTGCCGGTACTGCCCCACCATGCC-
 CCGGTGCCACGCGCGGGTAGTTACGGTGGGACCGGACACTCTCTCCGAGCGGGGACAGACTAGTGGCAGTTGTGGTAGACACCGCCGATGACGGGGTGGATCTGG-
 R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V M P V
 CCGTGTCTGAGGGGGTCTTGCCGGGCTGCTCAGGTGTGTGCACTACCGGATGTGGCTTCAGTCCATCCGGTCCCTGGCTGCCCGCGGGGCTGAACCCGCTG-
 GCGACAGCGTCCCGCAGACCGCGCGGACCGGAGTCCACACACAGTTGATGGGCTACAGCGGAGGTCAAGTAGCGCGAGGACCGACGGCGCGGCACTTGGGGAC-
 cctnagg(NstII)
 V S Y A V A L S C Q C A L C R S T T D C G G P K D M P L T C D D P R G S
 GTCTCTACGCGGTGGCTCTCAGCTGTCAATGTGCACTGCGCGCGGACGACACTGACTGGGGGGTCCCAAGGACACCCCTTGACCTGTGATGACCCCGCGGGATCC-
 CAGAGGATGCGGACCGACAGTCCAGACTACAGCTGAGACGGCGGGGTCGTGGTGACTGACGCGCCCGCCAGGGTTCCTGGTGGGGAATGGACACTAGTGGGCGCCCTAGG-
 (SstII)ccg-9999atcc(BamHI)
 G S G S G S A P D V Q D C P E C T L Q E M P F F S Q P G A P I L Q C M G C
 GGTAGCGGATCTGGTAGCGCTCTGATGTGAGGATGGCGGAGATGGCGGAGATGGACGCTACAGGAAACCACTTCTTCCAGCGGGTCCCCAATCTTCACTGATGGCTGG-
 CTAATCCCTAGACCATGCGGAGGACTACAGCTCTAACGGGTCTTACGTGCGATGCTCTTTTGGTAGAGAGAGGGTCCGCCACGGGGTTATGGAAGTCAGTACCGCGACG-
 agcgcT(EcoRII)
 C F S R A Y P T P L R S K K T M L V Q K M V T S E T C C V A K S Y M R V
 TGTTCTTAGAGCATATCCCACTCCACTAAGGTCCAGAGCATGTTGGTCCAAAGAGCTCAGCTCAGAGTCCACTTGGTGTGTAGCTAATCATATACAGGGTC-
 ACGAGAGATCTGTATAGGGTAGGTGATTCAGGTTCTTCTGTACACACAGGTTTCTTGGAGTGGAGTTCAGGTGAACGACACATCGATTAGTATATGTCCAG-
 T V M G G F K V E M N T A C H C S T C Y Y N K S *
 ACAGTAATGGGGGTTTCAAAGTGGAGAGCACACGGGTGCCACTGCACTGTTATATATACAAATCTTAGGTACC-3'
 TGTCAITACCCGCCAAGTTTCACCTCTTGGTGTGCCGACGGTCACTCATGAACAATATAGTTTAGAATTCATGG-5'
 99tccc(KpnI)

Figure 7

Coding Sequence for Single Chain Gonadotropin Analog #3 and Primers (underlined)

5'-ATGAAATCGAGCGAATCAGACTCGAGCGAGGAATGGAGATGGTCTGAGGAGGCTGGTCTGAGGAGGATGGGATCCAGGAGCGCGCTT-
 3'-GGTTCCTTACCTCTACGAGGTCCTCCGACGACGACGACGAGCTGCTAGCCGCCCGCTACCGTAGGTCCCTCGGCGAA-
 ctgag(MhoI)

M E M L Q G L L L L L L S M G G A W A S R E P L

R P W C M P I M A I L A V E K E G C P V C I T V M T I C A G Y C P T M M

CGCCATGGTCCACCCCATCAATGCCATCGCTGGTGGAGAGAGAGGCTGCCCGCTGTGCATCACCCTCAACACCAACCATCTGTGCCGCTACTGCCCCACCATGATC-
 GCCGTACCACGGATGGGATGTTACGGTAGGACCGACACTCTTCTCCGACGGGCGACAGCTAGTGGCAGTTGTGGTAGACAGGCGCGATGACGGGGTGGTACTAC-

R V L Q A V L P L P Q V V C T Y R D V R F E S I R L P G C P R G V D P V

CGGTGCTGAGAGCGGTCTGTGCCCGCTCTCAGGTGGTGTGCACCTACCGTGGTGGCTTGGAGTCCATCGGCTCCCTGGCTGCCCGGTGGGTGGAGCCCGTG-
 GCGACGAGCTCGGCCAGAGCGCGCGGACCGAGTCCACACACAGTGGATGGACTACAGCGGAGGCTCAGTAGCCGAGGACCGAGCGGCGACCGGACCTGGGCGAC-

cctnagg(MatII)

V S F P V A L S C R C G P C R S T S D C G G P K D H P L T C D H P Q G S

GTCTCTTCCCTGTGGCTCTCAGCTGTGCTGTGAGCCTTCCGCGCGAGCAGCTCTGACTGTGGGGTCCCAAGACACCCCTTCACCTGTGACACCCCGCCAGGATCC-
 CAGAGGAGGGGACACCGAGTCCAGACGACACTGGGACGGCGGCTGCTGGAGACTGACACCCCGCGGTTCTGGTGGGAGCTGGACACTGGTGGGGTTCCTAGG-

(BamHI)ggatcc

G S G S G S A P D V Q D C P E C T L Q E M P F S Q P G A P I L Q C M G C

GGTAGCGATCTGGTAGCGCTCTGTGATGTCCAGGATGCCAGGATGGCTACAGGAGAGAGGCTTCTTCCAGCGCGGCTGCCCAATCTTCAGTGCATGGGCTGC-
 CCATCCCTAGACCATCGCGAGGACTACAGCTCTACCGGCTTACGTCGGATGCTCTTTGGGTAGAGAGAGGCTGCCCGCGGCGGTTATGAAGTCCAGTACCGGAGC-

ggcgt(EcoRII)

C F S A V P T P L R S K K T M L V Q K M V T S E S T C C V A K S Y N R V

TGCTTCTAGAGCATATCCCACTCCCACTAGGATAGGATCCAGAGAGAGGATGTTGGTCCAAAGAGAGCTCAGCTCAGAGTCCATCTGTGTAGTAAATCATATACGGGTG-
 ACAGAGAGATCTGTATAGGATGAGTGATTCAGGTTCTCTGTACAGACGAGTTTCTTCCAGTGGAGTCTCAGGTGAACGACACATCGATTAGTATATGTCGAG-

T V M G G F K V E M H T A C H C S T C Y Y N K S *

ACAGTAATGGGGGTTTCAAGTGGAGAGCACAGGGGTGCCACTGCACTTGTATATATCAGAAATCTTAGGTACC-3'

TGTCATTACCCCGCAAGTTTCACCTCTTGGTGTGCCGACGGTGCAGTCAAGCAATATAGTGTTCAGATTCCTATGG-5'

ggatcc(KpnI)

Coding Sequence for Single Chain Gonadotropin Analog 4 and Primers (underlined)

5'-ATGAAATGACGGGATGACACTGACGACCAAGGATGAGGACATCGATTTTCTCTTTCTGTTCTGGGAAGCAATCTGCTGCATAGCTGTGACCTGACCAAC-
M K T L Q F F F L F C C W K A I C C N S C E L T N
3'-GATCTACTCTCTGAGGTCAGAAAGAGCAAGCAAGCACTTTTGGTTAGACAGCGTTATCGACACTGACTGCTGTG-
ctcgag(XhoI)

I T I A I E K E E C R F C I S I M T I W C A G Y C V T R D L V Y K D P A R
 ATCACCATTGCATTAGGAAGAAGATGTCTTTGCTATAGCATCAACCACTTGTGTGTCTGCTACTGCTACACGAGGATCTGGTGATAAAGCAACCCACGCCACG-
 TAGTGGTAGCTATCTCTTCTTACAGCAAGAGCTAGGCGTAGTGTGGTGAACCAACACGACCGATGACGATGTGCTCCCTAGACCAATATCTTGGGTGGTCC-
 P K I Q K T C T F K E L V Y E T V R V P G C A H A D S L Y T Y T V A T Q
 CCCAAATCCAGAAACATGTACCTTCACGAACCTGGTATATGAACAGTGAAGAGTGCCTGGGTGTCTCACCATCGAAGATCCCTGTATACATACCCAGTGGCCACCCAG-
 GGCTTTTAGGTCTTTGATACATGGAAGTTCCTTGACCATATCTTGTCACTCTACGCGGCACACGAGTGGTAGCTTAAGCAACATATGTATGGGTACCCGGTGGGTCT-
 Tggcca(Ball)

C W C G K C D S D S T D C T V R G L G P S Y C S F G E M K E G S G S G S G
TGTCACTGTGGGAAGTGTACACGACGACCTGATGTACTGTGGAGGCTGTGGGGCCGAGCTACTGCTCTCTTTGGTGAAGAAGAACGACCTCCGGTAGCGGATCGTGT-
ACAGTGAACACGCTTCCAGCTGTCCGTGTGTGACTTACATGACACGCTCCGAGCCCGGGTGGATGACGAGGAACCACTTACTTCTCTTAGGCACTGGCTAGACCA-
ggggccc(ApaI) ggagccc(BamHI)

S A P D V Q O C P E C T L Q E N P F F S Q P G A P I L Q C M G C C F S R A
ACGCTCTGATGTGCAGATGCCAGATGCAGCTACGAAACCAATCTTCTCCAGCGGGTCCCACTACTTCATGTCATGGCTGCTCTCTTAGGCA-
TCCGAGAGACTACACGTCCTACGGGCTTACGTGCATGTCTTTTGGGTAGAAGAGGGTCGGCCACCGGGGTATGAAGTCAAGTACCCGACGACCGAGGATCTCTG-
ggcgcct(Eco47III)

Y P T P L R S K K I M L V Q K N V T S E S T C C V A K S Y N R V T V M G G
TATCCCACTCACTAGGTCCAGGAGGACGATGTTGGTCCAAAGAGCGTCACCTCAGGTCCACTTGTGTGTAGTAAATCATATACAGGCTCAGATTAATGGGGGT-
ATAGGCTGAGGTGATTCACAGGTCTCTGCTACACACAGGTTTCTTGCTGAGTGGAGTCTCAGGTGAACGACACATCGAATTAGTATATTGTCAGGCTGTCAATTAACCECCA-

F K V E N H T A C H C S T C Y V N K S *

TTCAAGTGGAGACCAACGGGTGCCACTGCAGTCTGTTATATACCAATCTTAGGTACC-3'

AAGTTTCACCTCTTGGTGTGCCGACGGTGATCATGAACAAATAGTGTTTAGATTCATGG-5'

ggtecc(kg)

Coding Sequence for Single Chain Gonadotropin Analog #5 and Primers (underlined)

5'-ATGAATCGAGGAATCAAGACTCGAGCCAGAGTGGAGATGTTCCAGGGGTTCTGCTGCTGCTGAGCATGGGGGGGACATGGGGCATCCAGGAGGCCCTT-3'-GGTCTACTCTACAGAGTCCCGACGACGACAGGAGCAGTCTGTAACCGCCCTGTACCCGTAGGTTCTTCGGCGAA-ctcag (XhoI)

R P R C R P I N A T L A V E K E G C P V C I T V M T I C A G V C P T M T
CGGGACACGGTGCCTGCCCATTCATATGCACACCTGGCTGTGGAGAGAGGGGTGCCCTGTGCATCAGCTCAGACACACCATCTGTGCCGGTACTGCCCCACCATGACC-
GCCGGTGCACACGCGGGGTAGTTACGGTGGGACCCGACACCTCTCTCCGACCGGGGACACGTAGTGGGATGTGGTGGTAGACAGGGCGCATGACGGGGTGGATCTGG-

R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V M P V
CGCGTGTGCAGAGGGGATCTGCCGGCTCTCAGATGTGTGCAGTATCCGCGATGGCTGTGGCTTCCAGTTCATCCGGTCCCTGGCTGCCCGCGCGGGCTGAACCCCGTGG-
GGGACACAGCTCCCCGACGAGCGCCGGGACGGATCCACACGATCTGATGGGCTGTACGCTGGAGCTCAGGTAGCGCGAGGGACCGACGGGCGCGCGCGCTCTTGGGGCAC-

cctnaga(Nat11)

V S Y A V A L S C Q C A L C D S D S Y D C T V R G L G P S Y C S F G E M K
G T C T C T A G C C G G C T C A G C T G C A A T G T C A C T C G C A G C A G C A G C A C T C A T T G T A C T G C G A G G C C T G G G G C C A G C T A C T C C T T T G G T G A A T G A A -
C A G A G A T C G C G C A C C G C A G T G C A G T T A C A G C G T G T C G T G T G A C T A A C A T G A C A G C T C C G G G T C G A T G A C A G C A G G A A C C A C C T T T T A C T T T -
gagccc (Apal)

E G S G S G S G S A P D V Q D C P E C T L Q E N P F F S Q P G A P I L Q C
G A G G A T C C G G T A C C G G A T C G T A G C G T C T G A T G T G A G A T T G C C A G A T G C A C G T A C A G G A A A C C A T T C T C C C A C G C G G G T G C C C A T A C T T C A G T G C -
T T C T T A G G C A T C G C T A G A C C A T C C G A G S A C T A C A G T C T A C G G G T T A C G T G C G A T G C T T T T G G G T A G A G A G G G T C G G C C C A C G G G G T T A T G A T C A G C -
g g a t c c c (BamH I) a g c g c t (Eco47111)

W G C C F S R A Y P T P L R S K K T M L V Q K N V T S E S T C C V A K S Y
 ATGGGGTGGCTGCTCTAGAGCATATCCCACTCCACTAAGTCCAGAGACGATGTGGTCCAAAGACGTCACCTCAGAGTCCACTTGGTGTGTAGCTAACTAATCATAT -
 TACCCGACGACGAGAGATCGTATAGGGTGGGTGATTCGAGGTCCTCTGCTACACCGAGGTTTCTTCGATGGAGTTCAGGTCAGCGACACATCGATTAGTATAT -

M R V T V M G G F K V E N T A C H C S T C Y Y N K S *
 AACACGGGTCACAGTAATGGGGGGTTCCAAAGTGGAGAACACACGGGTCGACTGCTATTATACAAATCTTAGGTACC-3'
 TTGTGCECAGTGTCATTACCCGCCCAAGTTTCACCTCTTGCTGTCGCCACGGTGACGTCATGACAAATAAGTGTTCAGATTCCATGG-5'
 ggTacc(Kpn)

Coding Sequence for Single Chain Gonadotropin Analog 46 and Primers (underlined)

(146) 330188

Coding Sequence for Single Chain Gonadotropin Analog #7 and Primers (Underlined)

5'-ATGGAATCGAGCGAATCAGACTCGACGACAGGATGGAGATGTTCTGAGGGGCTGCTGCTGTCTGAGCATGGCGCGGACATGGGATCCGAGGAGCGCTT-
3'-GATTCCTACCTCTACAGGTCCCGGACGACGACGAGGACGACTCGTACCGGCGCTGTACCGGTAGTTCCTCGGGGGA-
ctcpgg(Kho1)

R P R C R P I N A T L A V E K E G C P V C I T V N T T I C A G V C P T M T
 C G G G C A G G T G C G C C C A T C A A T G C A C C T T G C T G T G A A G A G G C G T C C C G T G C A T C A C G T C A A C A C A C C A C T G T G C C G G T A C T G C C C A C C A T G A C C
 G C C G G T G C C A C G C G C G G G T A S T T A C G G T G G G A C C G A C A C T C T T C C T C C G A C G G G G A C A C A C T A G T G G C A T T G T G T A G A C A C G C C G A T G A C G G G T G G A T C G G
 R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V N P V
 C G G T G T G C A G A G G A T T C G C G G C C T G C T C A G A T G T G T G C A A T A C C G G A T G T G C G C T T C A G T C A T C C G G T C C C T G C T G C C G C G C G G C T G A A C C C G T G
 G G C A C A C A T C C C C A G A G A C G C G G A G A C C A T C A C C A C A C T G A T G G C G T A C A C G G A G T C A G T A G G C G A G G A C G A C A C G G G C G C G C C G A C T T G G G G C A C
 cctnaga (NstII)

V S Y A V A L S C Q C A L C R R S T T D C T V R G L G P S Y C S F G E G S
GTCTCTACGCGTGCTCTACGTGTCAATGTGACTCTCCGCCGACGACACTGACTGCACCTGCGCAGCCTGGGCCGAGCTACTCTCTTTGGTGAAGATCC-
CAGAGGATCGCGCACCGCAGCTGCAGCTTACATGTGACAGCGCGGCTGTGTGACTGACGTGACAGCTTCGGACATCCCGGGTCGATGACGACGGAAACCACTCTCTAGG-
ggatccc(ApaI) ggatccc(B

G S G S G S A P D V Q D C P E C T L Q E M P F F S S Q P G A P I L Q C M G C
GGTAGCGGATCTGTAAGCGTCTGATGTGAGATGTCAGATGCAAGTACAGAGAAACCCATCTCTCCAGCCGGGTGCCCAATCTCATGTCATGGGTGC-
CATTCGCTAGACCATCGCAGGACTACAGTCTTAAGGGTCTTAAGTGCAGTGCTCTTTGGTAGAGAGGGTGGGCCACGGGGTTATGAATGATCATGCACTACCCGACG-
agcgcct(Eco47III)

C F S R A Y P T L R S K K T M L V Q K N V T S E S T C C V A K S Y M R V
GCTCTCTAGAGCATATCCCACTCCATAGGTCGACGAGGACATGTGGTCNAAAGACGTCACTCAGAGTCCACTTGTGTAGCTAAATCATATACAGGTC-
ACGAGACATCTCGATAGGGTAGGTCATCCAGGTTCTTCTGTCACACCAAGGTTCCTTCCAGTCGAGCTCAGGTGAACGACACATCGATTAGTATATTGTCGAG-

Y V M G G F K V E N H T A C H C S T C Y V M K S *

5'-CAGTAAATGGGGGTTCAAAGTGGAGAACACACGGGGTGCACATGCAGTACTTGTATTATCACAAATCTTAGGTACC-3'
5'-GTCATTATCCCCCAAAGTTACCTCTTGGTGTCCCGACGGTGACGTCATGAACAAATAATAGTGTTAGAATTCATGG-5'

99tacc(Kpnl)

Coding Sequence for Single Chain Gonadotropin Analog #8 and Primers (underlined)

5'-ATGAGATGACGCAATCAAGCTCGAGCCAGATGAGAGATGTCAGGGGGTGGTCTGTCTGTCTGATGATGGGGGGACATGGGGCATCGAGGACCTCTT-3'-GGTTCTTACTCTTACAGAGTCCCGACGACGACGACGACGACCTCTTACCCGCGCTGTACCGGTAGGATCTCTGGGGA-ctcgaag(XhoI)

R P R C R P I M A T L A V E K E G C P V C I T V N T I I C A G V C P T M T
CGGCCACGGTGCCECCCATCATGCCACCCCTGGCTGTGGAAAGAGGGCTGCCCGTGATCACCCTCACCACACACCATCTGTGCCGGCTACTGCCCCACCATGACC-
GCCGGTGCACACGCGGGGATTTACGGTGGACACGACACTCTCTCTCCGACGGGGCACACGTAGTGGCAGTTGTGTGTATACACGGGCGATGACGGGGTGGATCTGG-
R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V M P V
CGCGTGTGCAGGGGGTCTGCCGGCTTGCCTCAGGTGGTGTGCACCTACCGCATGTGGCTGTCCAGTTCATCGGGTCCCTGGCTGCCGGCGGGCTGACCCCTGTG-
GGGCACGACGTCCCGAGAGAGGCGGGACGGATCCACGACAGCTTGAATGGCGCTACACGGCAAGCTCAGTAGGCGGAGGACGACGGGCGCGCCGCACCTTGGGGCAC-
ccnnagg(Nat11)

V S Y A V A L S C Q C A L C R S T I D C T V R G L G P S Y C D D P R G S
G T C T C T A C C G C G G T C T C A G C T G C A A T G C A T T G C A C C A C C T G A T G C A T G C G A G C C T G G C C C A C C T A C T G C C A T G C C C C G G G C A T C C -
C A G A G G A T C G C G C A C C G A C A G T G C A C A G T T A C A G T G A G A C G G C G G C T G T G G T G A C T G A C G T C C G A C C T C C G G G T C G A T G A G C T A C T G G C G C C C T A G G -
999ccc(Apal) (Sall)ccgcggggatccc(BamHI)

G S G S G S A P D V Q D C P E C T L Q E N P F F S Q P G A P I L Q C M G C
GGTACGGCATCTGATAGCGCTCTCATGTGCAGATATGCCAGATGCACGCTACAGGAAACCATCTCTCCACGCGGGTGCCTCACTTCAGTGCATCGGCTGC-
TCGATCGCTACGACCATCGACGAGCATACAGCTCTTACCGGGTCTTACGTGGATGTCTTTTGGGTACGACAGAGGGTGGGCCCGCAGGGGTTATGAGTCAAGTACCCGAGC-
agc-gct(Eco47111)

C F S R A V P T P L R S K K T M L V Q K N V T S E S T C C V A K S Y N R V
TGCTTCTAGACGATATCCCACTCCCACTAGGTCACGAGACGATGTGGTCMAAGACGTCACTCAGAGTCCACTTGTGTGCTAGCTAACTATACAGGGTC-
ACGAGAGGATCTGTATAGGTCAGGTCATTCAGGTTCTCTGCTACACCGAGGTTTCTGTCAGTGGAGCTCTCAGGTGACGACACATCGATTTAGTATATGTCCGAG-

T V M G G F R V E N H T A C H C S T C Y Y H K S .

ACAGTAAATGGGGGTTTCAAGTGGGAACACACACGGGTGCCACTGCAGTACTTGTATTATACACAAATCTTAAGGTACC-3'
TGTCAATACCCCCCAAAGTTTCACTCTTGGTGTGCCGACGGTGAAGTCATGAACAAATAATAGTGTTTAGAAATTCATCGG-5'

ggtaacc(kpnl)

Coding Sequence for Single Chain Gonadotropin Analog 9 and Cassette (underlined)

5'-ATGAATCGACGGATCGACGACGAGTGAAGACACTCGAGTTTCTCTTTCTGTTCTGGAAGCAATCTGCTGCACTAGCTGTGAGCTGACCAAC-
M K T L Q F F F L F C C W K A I C N S C E L T M
3'-GATTCCTACTCTGTGAGGTCAAAAAGAGAAAGACAGCAGCTTTCTGTTAGAGAGCCTTATCGAGACTGACTGCTGTG-
ctgaa (XhoI)

I T I A I E K E E C R F C I S I M T I V U C A G Y C Y T R D L V Y K D P A R
 ATCACCATTGCATAGAGAAGAGATGCTTTCTGCATATGCATCAGACCACTTGGTGTCTGGTACTACTACACAGGAGTCTGGTGTATAGAGATCCAGCCAGG-
 TAGTGGTACGTTATCTCTCTTACAGCAAGACGTAGGCTAGTGTGGTGAACACACAGCCGATGACGATGGTCCCTAGACCAACATATCTTGGATCGGTC-
 P K I Q K T C T F K E L V Y E T V R V P G C A H N A D S L Y T V T V A T Q
 CCAAAATCCAGAAACATGTACCTTCAGGAACCTGGTATATGAACAGTGAAGTGCCTCCAGATCGAAGTCTCTGTATACATACCAATGGACGCCAGC-
 GAGTTTATGGTCTTTGTACATGGAAGTTCCTTGACCATATCTTTGTCACTCTCAGCGGCCAGACAGTGGTAGCTCTAAGGAACATATGATGGGTACCCGGTGGGTCT-
 TGGCCA (8a11)

C H C G K C D S D S T D C T V R G L G P S V C S F G E G S G S G S A P
TGTCACTGTGGCAAGTGTACACGACAGCACTGATTGACTGTCCGAGGCTGGGGCCAGCACTGCTTCTTTGGTGAAGGATTCGGTACGGGATCTGTAGCGCTCT-
ACAGTGAACCGCTTCACCTGTGCTGTGCTGACTAATGACAGCTTCGGACCTCCGGTTCATGATGAGGAACCACTTCTTAGCCATTCGCTAGACCATTCGGCAGG-
ggggccc(ApaI) (BamHI)ggatcc agcgcct(Eco4711II)

D V Q D C P E C T L Q E N P F S Q P G A P I L Q C M G C C F S R A Y P I
GATGTGAGGATTCGCAGATGCAACCTACAGAAACCACTTCTTCGACGCGGGTGCACAACTTCAGTCCA TGGGTGCTCTCTAGAGCAATCCACT-
CTACACAGCTCTACGGGCTTAGCTGCGATGTCCTTTGGGTAGAGAGAGGGTGCGCCACAGGGGTTTGAAGTCACGTACCGGACGACGACGAGATCTCTGATAGGGTGA-

P L R S K K I M L V Q K N V T S E S T C C V A K S Y N R V T V M G G F K V
CCCAATAGGTCGAAGAGACGATGTTGGTCCAAAGACGTCACCTCAGATGCCATCTGTGTAGCTAAACATATACACGGGTACACAGTAATGGGGGTTTCAAGTGTG
GGTGGATTCAGGTTCTCTGCTACACCAAGGTTTTCTTGCAATGGAGTCTCAGGTGAACGACACATCGATTTACTATATGTGCCAGTGTCAATTACCCCAAGGTTTTCAC-

E N H T A C H C S T C Y Y H K S *

GGAGAACACACGGGGTGCCTGCAGTACTTGTTATTACAAATCTTAGGTACC-3',
CTCTCTGGTGTGCGCCGCGGTGACGTCATGAAACATTAATAGTGTTAGAATTCATGG-5',

9912 acc (Kpn1)

Figure 14

Coding Sequence for Single Chain Gonadotropin Analog 10 and Cassette (underlined):

5'-ATGAAATCGAGGAATCAGACTCGAGCCAGGATGAAGCACTCCAGTTTTCCTCTTCTGCTGCTGGAAGCAATCTGCAATAGCTGTGAGTGAACAC-
 3'-GATTCTACTTCTGTGAGSTCAAAAGAGGAAAGACAGGACCTTTCTTTAGCAGACGTTATCGACACTCGACTGGTTG-
 ctgag(KhoI)

M K T L Q F F L F C C W K A I C C M S C E L T M

I T I A I E K E C R F C I S I N T I W C A G Y C Y T R D L V Y K D P A R
 ATCCATTGCAATAGAGAAAGAGAAATGTGTTCTTCATAGCATCAACCACTTGGTGTGCTGCTACTGTACACAGGGATCTGGTATAGGACCCAGCAGG-
 TAGTGGTAGCTTATCTTCTTCTTACAGCAAGAGCTAGGCTAGTGTGTGACCCACAGCCGATGCAATGTGTGCTCCCTAGACCAATATTCCTGGGTGGTCC-

P K I Q K T C T F K E L V Y E T V R V P G C A N H A D S L Y T Y P V A T Q

CCAAATCCAGAAACATGTACTTCAGGAAGTGTATGAACAGTGAAGTGGCCGGCTGTGTCACCATGCAGATTCCTGTATACATACCCAGTGGCCACCCAG-
 GGGTTTAGGCTCTTTGTACATGGAAGTTCCTGACCATATCTTGTCACTCTCACGGCCGACAGAGTGGTACGCTAGGCAACATATGTATGGTCACCGGTGGGTC-
 tggcca(BalI)

C N C G K C D S D S T D C T V R G L G P S Y C G S G S G S A P D V Q D

TGTCACTGTGGCAAGTGTACAGCAGCACTGATGTACTGTCCAGGCTCGGGCCCACTTCCGATCCGGTAGCGATCTGGTAGCGCTCTGTATGTGAGGAT-
 ACAGTGACACCGTTACACTGTGCTGTGCTGACTATACATGACACGTCGGGACCCGCTGAGGCTAGGCTAGGCTAGACCATCGGAGGACTACAGTCTTA-
 gggccc(ApaI) (BamHI)ggatcc agcctt(EcoRII)

C P E C T L Q E M P F F S Q P G A P I L Q C M G C C F S R A Y P T P L R S

TGCCAGAAATGCACGCTACAGGAAACCAATCTCTCCAGCCGGGTGCCCAATCTCAGTGCATGGGTGCTGCTCTCTAGAGCATATCCCACTCCACTAGGTCC-
 ACCGGCTTACGTGCCATGTCTCTTTGGGTAGAGAGGGTGGGCCCGGGGTTATGAAGTCAAGTACCCGACGAGAGATCTGTATAGGGTGAAGTGAATCCAGG-

K K T M L V Q K M V T S E S T C C V A K S Y M R V T V M G G F K V E M H T

AGAAGACGATGTGGTCCAAAGAGAGTCACTTCAGAGTCCACTTGTGTGTAGTAAATCATATACAGGATCAAGTAAATGGGGGTTTCAGAGTGAAGAACCAACG-
 TTCTTCTGTACAAACAGGTTTCTTGTGAGTGGAGTCTCAGGTGAACGACACATCGATTAGTATATTGTCCCAAGTGTATACCCCAAGTTTCACCTCTTGTGTGCTG-

A C H C S T C Y Y N K S *

GGTGGCACTGCAGTACTGTATTATACAAATCTTAGGTACC-3'
 CGCACGGTGAAGTCAATAGTATTAGATTCCATGG-5'

ggatcc(KpnI)

Figure 15

Preparation of an alpha-subunit coding region lacking oligosaccharide signal sequences

C G S G S G S A P D V Q D C P E C T L Q E M P F S Q P G A P I L Q C
TGGGATCCGTAAGCGATCTGGTACGCTCCTGATGTGACGAGTTCGCCAGATGCAGCTACAGGAACCCCATCTCTCCAGCGGGTGCCCAATCTTCAGTGC-
ACGCTAGGCCATCGCTAAGCAATCGGAGGACTACAGCTCTTACGCGATGCTTTGGTAGAGAGGGTCGCCGCCGGGTATGAGTCAGC-
(BamHI)ggatcc agcgctt(Eco47III)

M G C C F S R A V P T P L R S K K T M L V Q K Q V T S E S T C C V A K S Y
ATGGCTGCTGCTTCTAGAGGATATCCACTCCACTAAGGTCCAGAGAGGAGGATGTTGGTCCAAAGGAGGTCACTCAGAGTCCACTTGTGTAGCTAATCATAT-
TACCCGACGACGAGAGATCTGTATAGGCTGAGGTGATTCAGGTTCTCTGCTACAGCAGGTTTTCGTGAGTGGAGTCTCAGGTGAACGACATCGATTAGTATA-
tctaga(XbaI)

N R V T V M G G F K V E Q M T A C H C S T C Y Y H K S *
AACAGGTCACAGTAATGGGGGTTTCAAGTGGAGGACACACCGCGTGGCACTGGAGTACTGTATTATACAAATCTTAAGGTACC-3'
TTGTCAGTGTCAATTACCCCAAGTTTCACCTCGTGTGTGTGCGGACGGTCAGCTCATGAACATAATAGTGTAGGATTCGATGGCCAIG-5'
ggatcc(KpnI)

Figure 16

Preparation of a beta-subunit coding region lacking an-linked oligosaccharide signal sequences

5'-ATGAAATGACGGAATCAGACTCGAGCCAGGATGGAGATGTCCAGGGGCTGTCTGTCTGCTGAGCATGGCGGACATGGGCATCCAGGAGCCGCTT-
 3'-GATTCCTACCTCTACAGGTCCCGACGACGACACGACGACTCTACCGCCCTGTACCGTAGGTTCTCTGGCGAA-
 ctgag(KhoI)

R P R C R P I Q A T L A V E K E G C P V C I T V M T T I C A G V C P T M T
 CGGCCACGATGCTGCGCCCATCCAGCCACCCCTGGCTGTGGAGAGAGGGGTGGCCCTGTGATCAGCTGACACACCAATCTGTGCTGGCTACTGCCCCACCATGACC-
 GCGGTGCCACGGCGGGGTAGGTTGGTGGGACCGACCTCTCTCCGACGGGACACAGTGTGGTGTGATGACACGGCCGATCAGCGGGTGGATCTGG-

R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V M P V
 CGGTGCTGACAGGGGGTCTCTGCGGCCCTGCTCAGGTGTGTGCACTACCGCATGTGCGCTTCGAGTCCATCGGCTCCCTGGCTGCCCGCGGGGTGACCCCGTG-
 GCGACGAGTCCCCGAGGACGGCCGGAGCGAGTCCACACAGTTGATGGCGCTACAGCGGAAGCTCAGTAGGCTCAGGGATCCGACGGGCGCGCCGACTTGGGGCAC-
 cctnag(NstII)

V S Y A V A L S C Q C A L C R R S T T D C G G P K D M P I T C D D P R F Q
 GTCTCTACCGCTGGCTCTCAGCTGTCAATGCTACTCTGCCCGCGAGCAGCACTGACTGCGGGGTCCAGAGGACACCCCTTGACCTGTGATGACCCCGCTTCCAG-
 CAGAGATGCGGACCGACAGTCCAGAGTTACAGTCCAGCGGGGCTGTGTGATGACGCGCCCGAGGGTCTGTGGGGAATGGACACTACTGGGGCGGAGGTC-

D S S S K A P P S L P S P S R L P G P S D T P I L P Q G S G S G S
 GACTCTCTCTCAAGGGCCCTTCCCGCAGCTTCCAGCCCATCCCGACTCCCGGGGCCCTCGACACCCCGATCTCTCCCGAAGATCCGGTAGGGATCTGGTAGG-
 CTGAGGAGAGGAGTTTCCGGGAGGGGGTCCGAGAGTTCGGGTAGGGTGAAGGGCCCTGGAGGCTTGGGGTAGGGAGGGTTCCTAGGGCCATCGCTAGACCATCG-
 ggagcc(ApaI)
 ggatcc(BamHI) agc

A P D V Q D C P
 GCTCTGATGTGAGGATGGCCA
 CGAGGACTACAGTCTTACGGGT
 gct(Eco47III)

Figure 17

Coding Sequence for Single Chain Gonadotropin Analog #1a

5'-ATGAAATGACGAGATCAGACTCGACCAAGATGGAGATGTTTCAGGGGGTCTCTGTTCTGCTGAGCATGGCGGGACATGGGCATCCAGGAGGCCCTT-
c (cont'd)

R P R C R P I N A T L A V E K E G C P V C I T V M T T I C A G V C P T M T
G C C C C A C G A T G C T C C C C C A T C A A T G C A C C C T G C T G T G A G A G A G A G G C T C C C C C T G C A T C A C C G T C A C C G T C A C A C C A C C A T C T G T G C G G C T A C T G C C C C A C C A T G A C C
C C C C G T G C C A C C G C G G G G A T T A C G T G C C A C C G A C A C C T C T C C C G A C G G G A C A C G A T G T G C A T T G T G T G A G A C A C C G C C A T G A C G G G A T G A T C T G G

R V L Q G V L R A L P Q V V C M Y R D V R F E S I R L P G C P R G V M P V
G C C A T G C T C A G A G G A T C C T C C G C C C T C C C T C A G A T G G T G C A A T A C C G C G A T G T G C C T T C G A T C A T C C G G T C C C T G G C T G C C G C G C G G C T G A A C C C C G T G
G C C A C G A C A T C C C C A G A G C G C G G A G A C C T C A C C A C C A T T G A T G G C C T A A G C C G A A G C T C A G T A G G C C A G G A C C A C G C G G C G C G C C A T T T G G G G A C

ccn3aga (Natl1)

[illegible]

A P O V Q D C P E C T L Q E N P F S Q P G A P I L Q C M G C C F S R A Y
GGCTGATGTGCAGGATTGCCCAAGTACAGCAAAACCATTCTTCACACGGGGTGCCCCCATCTCAGTGCATGGGTGCTTCTCTAGACGATAT-
CCAGACTACACATCTTAACGGGTCTACGTGCGATGCTCTTTGGTAGAAGAGGGTGGCCCGACGGGTATCGAGTCAGTACCCGACGACGAAGAATCTCTATA-
ggct(cod7111)

P T P L R S K K T M L V Q K Q V T S E S T C C V A K S Y M R V T V M G G F
E C C C A C T C A C T A A G G T C A A G A A G C A G T T G T G C A A A G C A G T C A G A G T C A C T T G C T G T A G C T A A T C A T A T A C A G G G T C A C A G T A T T G G G G G G T T T C -
G G G T G A G S T G A T T C C A G S T C T T C T T G C T A C A C C A G G T T T C G T C A G T G A G C T C A G T G A A C A C A C T G A T T A G T A T T G T C C A G T G T C A T A T C C C C C T A A A G -

K V E G H I A C H C S I C Y Y H K S *

AAAGTGGAGCAACACACGGGGTGGCAGTACTTGTATTATCACAAATCTTAAGGIACC-3'

TTTCACCTCGTTGTGTGCCCGCACGGTGACGGTCAIGAACAAATAATAGTGTIIAGAAATCCATGGGCTAGGTAGAGATCCGATAGGGCCCT-5'

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